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REDUCING FALLS IN PARKINSON DISEASE

It is estimated that up to two thirds of patients with Parkinson disease (PD) experience falls each year. Postural instability is thought to be a significant cause of these falls. PD can be considered an acetylcholine-deficient state based on cholinergic cell loss in the nucleus basalis of Meynert (NBM) and in the pedunculopontine nucleus (PPN) - laterodorsal tegmental complex. In addition, medications with anticholinergic properties are associated with impaired balance, increased falls and increased rates of bony fractures in the elderly. This controlled trial explored the effects of an acetylcholinesterase inhibitor, donepezil, in subjects with PD who fall frequently.

The double-blind, crossover, clinical trial included patients diagnosed with PD. The inclusion criterion specified a baseline frequency of falling or nearly falling two or more times per week. Ambulatory patients were randomized to receive either placebo or donepezil at up to 10 mg per day. As the primary outcome measure, subjects completed postcards reporting falls or near falls. Secondary outcome measures included the Mini Mental State Exam, the Berg Balance Scale, the Motor Unified Parkinson Disease Rating Scale, the Activities of Balance Confidence Scale and a subjective global impression of change. Twenty-three subjects, with a mean age of 68.3 years, were initially randomized, with six subjects withdrawing due to drug side effects.

Those receiving donepezil fell significantly less often than did those receiving a placebo ($p=0.049$). The five subjects with the most frequent falls demonstrated the greatest reduction in falls while taking the study drug. No significant differences were seen between the groups on secondary outcome measures.

Conclusion: This study of patients with Parkinson disease found that a cholinesterase inhibitor, donepezil, can reduce the frequency of falls and near falls, without impacting cognition, balance or disease severity.

Chung, K., et al. Effect of Central Cholinesterase Inhibitor on Reducing Falls in Parkinson Disease. *Neurol.* 2010, October 5; 75(14): 1263-1269.

LOW-LEVEL NMR FOR POSTTRAUMATIC OSTEOARTHRITIS

Previous research has demonstrated that electromagnetic fields may improve bone development, increase chondrocyte proliferation and reduce cartilage damage. A number of studies have demonstrated that pulsed electromagnetic fields can improve recovery after arthroscopic treatment of cartilage lesions. This animal study sought to determine whether low energy nuclear magnetic resonance (NMR) may be beneficial in post traumatic osteoarthritis.

Twenty-four, mature white rabbits underwent transection of the anterior cruciate ligament. The animals were randomized into four groups, including those treated with NMR daily for seven days beginning six or 12 weeks after surgery, or to one of two control groups. One week after the last treatment, osteoarthritis was graded macroscopically and histologically.

The median macroscopic grade of OA after six weeks of treatment was superior to that of the control group ($p<0.01$). For the delayed (12 weeks) groups, no significant difference was seen between the treatment and control groups ($p=0.81$). The histological results further revealed no differences between the two groups.

Conclusion: This animal study found that low-level NMR, one hour per day within six weeks of ACL surgical rupture, may reduce the development of osteoarthritis.

Jansen, H., et al. Effects of Low Energy NMR on Posttraumatic Osteoarthritis: Observations in a Rabbit Model. *Arch Orthop Trauma Surg.* 2010DOI10.1007/s00 oh02-010-1205-1 - 4.

PROTECTING AGAINST KNEE OSTEOARTHRITIS

Osteoarthritis (OA) is a disease of both biomechanical and biochemical dysfunction. Impairments in quadriceps strength and proprioception have been linked to the development of knee OA. This study was designed to determine whether a combination of knee extension strength and knee joint position sense is important in protecting against the development of knee OA.

Three thousand twenty-six men and women, ages 50 to 79 years, each with either knee OA or with risk factors for knee OA, were enrolled in this multi-center study. Data collected included body mass index, knee extensor strength, joint position sense, knee radiographs, knee symptoms, physical activity and medical history. Measurements were taken at baseline and again at 30 months follow-up.

A multivariable logistic regression was completed, with the results revealing that greater knee extensor strength was associated with a decreased risk for incident symptomatic OA. This finding held true regardless of joint position sense after adjusting for age, body mass index and surgical history. No significant relationship was found between joint position sense and incident symptomatic knee OA.

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Conclusion: This study found that greater knee extension strength is associated with a decreased incidence of symptomatic knee osteoarthritis.

Neil, A., et al. Effect of Quadriceps Strength and Proprioception on Risk for Knee Osteoarthritis. **Med Sci Sp Med.** 2010. November; 42(11): 2081-2088.

EFFICACY AND SAFETY OF MORE INTENSIVE LOWERING OF LDL

Standard statin treatment typically reduces LDL cholesterol concentrations by about one third. Regimens involving higher doses may reduce LDL levels by one half. This meta-analysis sought to determine whether large reductions in LDL cholesterol can safely produce further reductions in major vascular events without significant adverse consequences.

This meta-analysis included trials focused on lowering LDL cholesterol with at least 1,000 participants and at least two-years follow-up. Outcomes included cause specific mortality, major coronary events, coronary revascularization, strokes, and new cancer diagnoses.

Data were reviewed from 26 trials including 170,000 patients. Comparing the less intensive regimens with the more intensive regimens, the more intensive regimens were found to produce a 15% further reduction in major vascular events, including reductions in coronary deaths or nonfatal myocardial infarctions, coronary revascularization, and ischemic strokes. Across the 26 trials included in the analysis, all cause mortality was reduced by 10% per 1.0 mmol/L reduction in LDL. No significant difference occurred between the groups in cancer incidence or cancer related deaths.

Conclusion: This meta-analysis found that aggressive reduction in LDL cholesterol can safely produce further reductions in cardiovascular events and death. A reduction in LDL cholesterol by 2 to 3 mmol/L produced a reduction in these risks by 40% to 50%.

Cholesterol Treatment Trialists Collaboration. Efficacy and Safety of More Intensive Lowering of LDL Cholesterol: A Meta-Analysis of Data

from 170,000 Participants and 26 Randomized Trials. **Lancet.** 2010, November 13; 376(9753): 1670-1681.

INTENSIVE LOWERING OF LDL CHOLESTEROL WITH 80 VERSUS 20 MG SIMVASTATIN

LDL cholesterol is an important cause of coronary heart disease. While previous studies have suggested that more intensive lowering of LDL cholesterol can produce reductions in adverse events, concern remains regarding potential side effects. This study sought to determine the safety and efficacy of long-term treatment with high-dose simvastatin.

This double-blind, randomized trial included 12,064 men and women 18 to 80 years of age with a history of previous myocardial infarction. The patients were randomized to receive either 80 mg or 20 mg daily of simvastatin. After randomization, the subjects were seen at two, four, eight and 12 months, and then at six-month intervals. The primary endpoint was major vascular events, including coronary death, myocardial infarction, stroke or arterial revascularization.

The patients were followed for a mean of 6.7 years. During that time, major vascular events occurred in 24.5% of those in the high dose group and in 25.7% of those in the low dose group (p=0.10). Compared with 20 mg simvastatin, allocation to 80 mg simvastatin was associated with proportional reductions of four percent in major coronary events, nine percent in any stroke and 23% in non-coronary revascularizations. More of the patients allocated to receive 80 mg simvastatin were likely to discontinue treatment due to increased liver or muscle enzyme concentrations, or to report muscle pain or weakness.

Conclusion: This study, comparing 80 mg and 20 mg of simvastatin daily, found that, among survivors of myocardial infarction, the higher dose results in a reduction in major vascular events, with a slightly higher risk of myopathy.

Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) Collaboration Group. Intensive Lowering of LDL Cholesterol with 80mg versus 20mg Simvastatin Daily in 12,064 survivors of Myocardial

Infarction: A Double-Blind, Randomized Trial. **Lancet**. 2010, November 13; 376(9,753): 1622-1624.

PREGNANCY RELATED CARPAL TUNNEL SYNDROME

The reported incidence of pregnancy related carpal tunnel syndrome (PRCTS) in the literature varies widely. Reports regarding the prognosis of PRCTS also vary considerably. This literature review sought to clarify the incidence and natural course of PRCTS.

The authors performed a literature review of studies published in Pub Med and Google Scholar, identifying 214 relevant studies. Of those, six met the study's inclusion criteria, including a consecutive series, an unequivocal definition of symptoms indicative of CTS, and a neurophysiologic assessment.

The reported incidence of neurophysiologically confirmed PRCTS ranged from seven percent to 43%. A rate of 17% was reported by three of the five studies. The incidence of clinically diagnosed PRCTS ranged from 31% to 62%. Symptoms persisted in 50% of the subjects at one year, and in 30% at three years.

Conclusion: This literature review suggests that neurophysiologically confirmed carpal tunnel syndrome occurs in approximately 17% of pregnancies, with symptoms persisting in 30% of these patients at three years.

Padua, L., et al. Systematic Review of Pregnancy Related Carpal Tunnel Syndrome. **Musc Nerve**. 2010, November; 42(5): 697-702.

SLEEP WAKE DISTURBANCES YEARS AFTER TRAUMATIC BRAIN INJURY

Sleep wake disturbances are common after traumatic brain injury (TBI), with previous studies demonstrating that this disturbance occurs in up to 72% of patients at six months post-injury. However, knowledge concerning the long-term outcome of posttraumatic sleep wake disturbance (SWD) is sparse. This study sought to better understand the long-term course of SWD in patients with TBI.

Sixty five patients, consecutively admitted to an inpatient TBI unit, were followed. None of the subjects reported a premorbid SWD or any psychological disorders. All were interviewed by phone after discharge concerning sleep quality and quantity. The questionnaires used included the Epworth Sleepiness Scale, the Sleep Apnea Scale of Sleep Disorders, the Beck Depression Inventory (BDI), several narcolepsy scales and the Fatigue Severity Scale (FSS).

Three years post-TBI, 78% of the patients consented to participation. Posttraumatic SWD was found in 67% of the patients, with posttraumatic hypersomnia seen in 27%, fatigue in 35% and insomnia in 10%. A significant relationship was seen between FSS scores and depression symptoms as assessed with the BDI ($p=0.001$), and between FSS scores and anxiety symptoms ($p=0.007$).

Conclusion: This prospective study found that, at three years after a brain injury, 67% of patients suffer from a sleep wake disturbance.

Kempf, J., et al. Sleep Wake Disturbance Three Years after Traumatic Brain Injury. **J Neurol Neurosurg Psych**. 2010, December; 81(12): 1402-1405.

CHRONIC PAIN IN GUILLAIN-BARRÉ

Guillain-Barré Syndrome (GBS) is characterized by the clinical triad of extremity weakness, paresthesias and areflexia. Pain, though known to be a component of the disease, has only been studied to a limited degree. This study investigated the intensity, type and location of pain complaints during the acute phase, and after recovery from, GBS.

This one-year, cohort study was completed with 170 patients diagnosed with GBS. Clinical data, biological materials and electrophysiologic data were collected systematically during the one-year follow-up. From these, pain symptoms, fatigue severity and disability over the course of the disease were determined.

Sixty-six percent of the patients reported pain during the acute phase, while 36% noted that pain began within two weeks of the onset of weakness. Patients reporting pain

during the acute phase had a higher severity of pain during the chronic phase. After one year, 38% of the patients still reported pain. In the chronic phase, pain intensity was correlated with the level of weakness ($r= 0.25$), functional disability($r= 0.51$) and fatigue($r= 0.52$). Pain was also more prevalent among patients who had sensory disturbances than among those with pure motor symptoms ($p<0.05$).

Conclusion: This study demonstrates that pain is a common symptom among patients with Guillain-Barré Syndrome, and that it is correlated with the degree of weakness and disability.

Ruts, R., et al. Pain in Guillain-Barré Syndrome: A Long-Term Follow-Up Study. **Neuro**. 2010, Oct; 75(16): 1439-1337.

OSTEOPONTIN PREDICTS LONG-TERM FUNCTIONAL OUTCOME AFTER STROKE

Osteopontin is an extracellular matrix protein which also acts as a potent inhibitor of soft tissue mineralization, thus enabling it to block ectopic calcification of the vasculature *in vivo*. Osteopontin is also a soluble cytokine involved in inflammation and tissue remodeling. During acute and chronic inflammatory responses, osteopontin further plays a functional role in early Th1 response.

It is thought that osteopontin serves to exacerbate inflammation in several chronic diseases, including atherosclerosis. However, a potential neuroprotective effect of osteopontin has been suggested in models of ischemia. Recent animal studies have demonstrated that the administration of osteopontin can cause a marked reduction in the size of an infarction after a transient middle cerebral artery occlusion. This study assessed human serum osteopontin levels after acute ischemic stroke.

Consecutive patients presenting within three hours of stroke symptom onset were recruited. All were scheduled for administration of tPA. Only those patients with a non-lacunar stroke involving the vascular territory of the middle cerebral artery were included. For all patients, a detailed history of vascular risk factors was obtained, with labs drawn to determine osteopontin levels. A

regression analysis was performed to determine which factors were associated with a poor prognosis.

The osteopontin level was increased among those patients who showed a worse outcome at three months. Logistic regression revealed that an osteopontin level of greater than 27.22 ng/ml was an independent risk factor for poor outcome, after adjusting for other potential confounders ($p < 0.006$).

Conclusion: This study of ischemic stroke found that elevated serum osteopontin levels drawn before the administration of tPA are independently associated with poor long-term outcome.

Mendioroz, M., et al. Osteopontin Predicts Long-Term Functional Outcome among Ischemic Stroke Patients. *J Neurol.* 2010; DOI: 10.1007/S00415-010-5785-z.

DEXTROMETHORPHAN PLUS QUINIDINE FOR PSEUDOBULBAR AFFECT

Pseudobulbar affect (PBA) is a neurologic condition characterized by involuntary outbursts of laughing and/or crying which are disproportionate to the patient's emotional state. This condition is thought to arise from disconnection of brainstem structures from cortical inhibition. In settings of amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS), dextromethorphan plus quinidine have been found to be beneficial in reducing PBA. This study further assessed the efficacy of this treatment.

This 12-week, randomized, double-blind, placebo-controlled trial included patients 18 to 80 years of age with a diagnosis of either ALS or MS and with clinically significant PBA. The subjects were randomized to receive either a placebo or dextromethorphan/quinidine 30/10 mg (high dose) or 20/10 mg (low dose). The primary efficacy outcome was the patients' change from baseline in the number of PBA episodes per day, as recorded in the patient's diary.

A total of 326 patients were randomized to complete this study. Over the course of the study, all three groups showed a substantial reduction in daily PBA episode rates relative to baseline. The PBA episode rate was 46.9% lower for the high

dose group, and 49% lower for the low dose group, than that for the placebo group ($p < 0.0001$ and $p < 0.0001$, respectively). Both dosages were well tolerated.

Conclusion: This study of patients with ALS or MS found that a combination of dextromethorphan plus quinidine can significantly reduce episodes of pseudobulbar affect.

Pioro, E., et al. Dextromethorphan Plus Ultralow Dose Quinidine Reduces Pseudobulbar Affect. *Ann Neurol.* 2010, November; 68: 693-702.

IMMUNE REGULATION OF MULTIPLE SCLEROSIS WITH THE MYELIN PEPTIDES

Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS), thought to be caused by a Th1 cell mediated immune response directed against CNS antigens. This leads to demyelination or clinical disability. Several attempts have been made to use antigen specific therapy for this disease. Animal studies have shown that, when applied transdermally, the immunodominant peptide of myelin ASIC protein can protect against autoimmune encephalomyelitis (EAE). This study tested a mixture of three myelin peptides applied transdermally to patients with relapsing remitting MS.

Thirty patients, ages 18 to 55 years, were included in this study. The subjects were randomized to one of three groups, to receive a placebo or to receive a mixture of either low dose or high dose of myelin peptides. The patches were changed once per week for four weeks and then once per month for 11 months. For each patient, the immediate responses in the skin, lymph nodes and peripheral blood immune cells were determined.

In the treated patients, dendritic Langerhans cells in the skin were activated, while a unique subpopulation of dendritic cells were induced in the lymph nodes draining the immunized area of the skin. In the periphery, the patches induced type I interleukin 10 producing Tregs and strongly suppressed myelin reactive T cell responses.

Conclusion: This study demonstrates that transdermally applied myelin peptides have

regulatory potential for the treatment of multiple sclerosis.

Jurynczyk, M., et al. Immune Regulation of Multiple Sclerosis by Transdermally Applied Myelin Peptides. *Ann Neuro.* 2010, Nov; 68 (5); 593-602.

RADIAL SHOCKWAVE VERSUS STRETCHING FOR PLANTAR FASCIOPATHY

Histological assessments of tissue from patients with chronic, painful plantar fascia reveal findings consistent with a failed healing response, without evidence of inflammation. Nonsurgical therapy is the mainstay in managing plantar heel pain, with treatments including heel pads, orthoses, corticosteroid injections, night splints and shockwave therapy. This study compared the efficacy of radial shockwave with that of stretch therapy for the treatment of patients with chronic plantar fasciopathy.

This study included 102 patients with painful plantar fasciopathy of less than six weeks duration. The subjects were randomly assigned to complete either a plantar fascia specific stretching program, performed three times per day for eight weeks, or to undergo three sessions of radial shockwave therapy at weekly intervals. At each shockwave session, 2,000 pulses were applied, with a total energy flux density per treatment of 320 mJ/mm². The treatment frequency was 8 pulses/sec. All participants completed the pain subscale of the Validated Foot Function Index and an outcome questionnaire at baseline and at two, four and 15 months.

While both groups reported an overall decrease in pain, an analysis of variance demonstrated significant effects of treatment and treatment - time interaction at two months, in favor of plantar fascia stretching. In addition, scores favored the stretching group in patient satisfaction at two months, and in activities of daily living at four months. No significant differences were seen between the two groups at 15 months follow-up.

Conclusion: This study found that a plantar fascia specific stretching routine, performed three times per day, is superior to a weekly

radial shockwave intervention for the treatment of plantar fasciopathy.

Rompe, J., et al. Plantar Fascia Specific Stretching versus Radial Shockwave Therapy as Initial Treatment of Plantar Fasciopathy. **JBJS**. 2010, Nov 3; 92(15): 2514-2522.

FUNCTIONAL ABILITY AFTER ABOVE THE KNEE AMPUTATION FOR INFECTED ARTHROPLASTY

Above the knee amputation (AKA) is a definitive treatment in patients who have a persistent infection after a total knee arthroplasty (TKA). The incidence of AKA after primary TKA is 0.10%. This study assessed ambulatory status and functional outcome after such surgery.

This retrospective study reviewed 35 patients at two institutions who underwent an AKA for treatment of an infected TKA. The AKAs were performed an average six years after the primary TKAs. Subjects were 19 females and 16 males with a mean age of 62 years. Functional status measures included SF - 12 and activities of daily living questionnaires after each surgery

During an average follow-up of 40 months post-surgery, two patients died in the immediate postoperative period, and 13 others died of causes unrelated to the septic joint. Nine patients required irrigation and debridement after the AKA, and two required an AKA stump revision. After AKA, 14 patients were fitted with prostheses. Of those, nine actually wore the prosthesis, with seven wearing it more than one hour per day. Three patients used the prosthesis only for transfers, whereas one patient never used the prosthesis. Eight patients were functionally independent outside of their homes.

Conclusion: This study of patients undergoing AKA after an infected TKA found that these patients tended to have low functional status, with only half walking after the AKA surgery.

Fedorcka, C., et al. Functional Ability after above the Knee Amputation for Infected Total Knee Arthroplasty. **Clin Orthop Relat Res**. 2010 DOI: 10.1007/s11999-010 -1577 -0.

PHANTOM LIMB SYNDROME USING PERIPHERAL NEURAL BLOCKADE

Phantom limb syndrome (PLS) has a prevalence of 60% to 70% at one year after amputation. Various surgical, pharmacologic and behavioral treatments have been attempted for the treatment of this syndrome, all with modest results. This prospective, observational study evaluated the efficacy of a prolonged infusion of a high concentration of a local anesthetic as an alternative to patient controlled analgesia with morphine.

This prospective study included 71 patients undergoing lower extremity amputation between 2004 and 2008. All subjects received a continuous infusion of 0.5% ropivacaine, starting during surgery and continuing for four to 83 days post-surgery. After discharge, the patients were instructed to assess for phantom limb syndrome weekly by withholding the infusion for 6 to 12 hours and documenting the presence of any significant phantom or stump pain. If these symptoms occurred during the withholding period, the infusion was restarted for another week.

On postoperative day one, 94% of the patients reported significant phantom pain, with 100% reporting significant stump pain. At 12 months postoperatively, 84% reported no phantom or stump pain, while ten percent reported mild pain, three percent reported moderate pain, and three percent reported severe pain. Phantom sensation decreased from 92% at one week to 39% after 12 months. Only six percent of the patients required opioid treatment after infusion discontinuation.

Conclusion: This study found that continuous peripheral nerve blockade for long durations postoperatively may be an effective strategy for the reduction of the occurrence of phantom limb pain after lower extremity amputation.

Borhi, B., et al. The Use of Prolonged Peripheral Neural Blockade after Lower Extremity Amputation: The Effect on Symptoms Associated with Phantom Limb Syndrome. **Anesth Analgesia**. 2010, November; 111(5): 1308-1315.

SPORTS ACTIVITIES AFTER TOTAL SHOULDER ARTHROPLASTY

A number of articles describe sporting activity after hip, knee or ankle joint replacement. However, far fewer studies have focused on activities after shoulder arthroplasty. This study sought to determine sporting abilities before and after total joint replacement.

Between 2003 and 2006, 155 anatomical total shoulder prostheses were implanted in 139 patients. Those who had bilateral surgeries, or were unable to complete a questionnaire, were excluded from the study. A total of 100 patients were included with complete data. Prior to surgery, all patients were administered a questionnaire concerning current sporting activity and restrictions thought to result from shoulder dysfunction. Also recorded was history of sports participation, sports participation before and after surgery and change in sporting activity.

Before shoulder disease onset, 55 of the 100 patients reported sports participation. A total of 89% of those patients were able to participate in sports at a mean of 2.8 years post-surgery. No subjects reported having to discontinue sporting activity as a result of surgery. Thirty-seven percent of the participants reported that they still suffered restrictions in their sporting activities due to continued shoulder problems. Twenty of the patients (40%) reported no restriction in sporting activity after surgery.

Conclusion: This study of patients undergoing total shoulder arthroplasty demonstrates that the probability of being able to participate in sports after surgery is high.

Schumann, K., et al. Sports Activity after Anatomical Total Shoulder Arthroplasty. **Am J Sp Med**. 2010, October; 38(10): 2097-2105.

MILD TRAUMATIC BRAIN INJURY AND FATIGUE

Fatigue is one of the most common symptoms of mild traumatic brain injury (MTBI), with a prevalence of between 22% and 59% at three months. This study sought to clarify the relationship between depression and post-MTBI fatigue.

Participants were recruited from among patients presenting with MTBI at a single hospital in New Zealand. Patients were excluded from participation if they had an abnormal CT scan. All subjects were assessed with the Fatigue Severity Scale (FSS), the Rivermeade Post-Concussion Symptoms Questionnaire (RPSQ), the Hospital Anxiety and Depression Scale, and the Vitality Scale of the Short Form-36 Health Survey, Version II. All consented participants were assessed no later than 10 days after injury, and again at three and six months.

Data were completed for 180 individuals. For those subjects, post-MTBI fatigue was noted in 68% at one week, 38% at three months and 34% at six months. The patients' fatigue related behaviors were interpreted by family as laziness in 30% of all participants at each interval.

Conclusion: This study found that fatigue is a persistent symptom of mild traumatic brain injury, which diminishes over the first three months and then becomes stable.

Norrie, J., et al. Mild Traumatic Brain Injury and Fatigue: A Prospective, Longitudinal Study. *Brain Inj.* 2010, December; 24(13-14): 1528-1538.

MORTALITY AMONG PATIENTS WITH FIBROMYALGIA

Fibromyalgia (FM) is characterized by widespread pain and multiple tender points. FM is also associated with multiple medical comorbidities, such as hepatobiliary disease, cerebrovascular disease, exercise intolerance and depression. However, few studies have examined the effects of FM on mortality. Thus, this Danish study assessed the effects of FM on mortality.

This prospective cohort included 1,361 patients diagnosed with fibromyalgia. All had been referred during the period from 1984 to 1999. Medical records were collected and reviewed to examine whether the patient fulfilled the American College of Rheumatology criteria for FM. In addition to information concerning smoking habits, medical diagnosis was obtained from the medical records. A personal identification number was used to link to the Danish mortality register. Standardized mortality ratios of

observed to expected deaths were then calculated.

Of the patients, 1,189 fulfilled the criteria for FM. The cohort was followed for a total of 5,295 patient years. No increase was seen in overall mortality among patients with FM compared to the general population. However, for females, an increased risk of death was noted due to suicide, liver cirrhosis/biliary tract disease and cerebrovascular disease. No such relationship was observed for the male patients.

Conclusion: This prospective study found that fibromyalgia is not related to an overall increase in mortality, although, for females, it is related to a higher risk of mortality from suicide, liver disease and cerebrovascular disease.

Dryer, L., et al. Mortality in a Cohort of Danish Patients with Fibromyalgia: Increased Frequency of Suicide. *Arthr Rheum.* 2010, October; 62(10): 3101-3108.

DOCOSAHEXAENOIC ACID AND COGNITIVE DECLINE IN ALZHEIMER DISEASE

Previous studies have shown that consumption of the omega-3 fatty acid docosahexaenoic (DHA) reduces the risk of Alzheimer disease (AD) and modifies the expression of Alzheimer's-like brain pathology in mouse models. This study sought to determine whether DHA supplementation can slow the rate of cognitive and functional decline among individuals with AD.

This randomized, double-blind, placebo-controlled trial included 402 individuals with mild to moderate AD. The patients were randomly assigned to receive either a placebo or DHA at a dose of 2 g per day. Subjects were assessed for rate of change over 18 months using the Cognitive subscale of the Alzheimer Disease Assessment Scale (ADAS-cog) and the Clinical Dementia Rating (CDR) Sum of Boxes. Secondary outcome measures included changes in scores on the Mini Mental State Examination and in activities of daily living, Neuropsychiatric Inventory (NPI) scores, and Quality of Life Alzheimer Disease Scale scores. Outcome measures were obtained at baseline, and then again at six, 12 and 18 months.

The effect of DHA treatment did not differ from that of the placebo on either of the primary outcome measures. The mean rate of change in ADAS-cog score over 18 months was 8.27 points for the placebo group, as compared with 7.98 points for the DHA group ($p=0.41$). The rate of change on the CDR Sum of Boxes over 18 months was 2.93 for the placebo group, as compared with 2.87 for the DHA group ($p=0.68$). In addition, there was no benefit of the treatment with DHA as measured by any of the secondary outcome measures.

Conclusion: This study did not find that supplementation with docosahexaenoic acid slows the progression of cognitive and functional decline among patients with AD.

Quinn, J., et al. Docosahexaenoic Acid Supplementation and Cognitive Decline in Alzheimer Disease. *JAMA.* 2010, November 3, 304; 4(17): 1903-1911.

COUNSELING AND PREPACKAGED MEALS FOR WEIGHT LOSS

In the United States, among adults, the prevalence of overweight and obesity combined is 68%. This problem is associated with excessive mortality and morbidity. While commercial weight-loss programs are popular, very few studies suggest that these programs have the potential to promote weight loss that exceeds that of office-based counseling or medical interventions. This study compared the effectiveness of a structured diet program with prepared meals to that of traditional counseling.

Eligibility criteria included an age of 18 years or older, a body mass index of 25 to 40 and a minimum of 15 kg over ideal weight. A total of 446 women were randomly assigned in a 3:3:2 allocation to a center-based intervention, a telephone-based intervention, or a usual care group. The control group received traditional weight-loss counseling concerning diet and exercise, including sample meal plans, recommendations to increase physical activity, written materials and resources, monthly follow-ups and a repeat counseling session at six months. The interventional groups received free prepackaged meals, with an eventual

transition to a meal plan prepared by the participants after one year. Exercise was encouraged for all participants. Patients were evaluated at six, 12 and 24 months for anthropometric data, cardiopulmonary fitness, quality of life and biochemical profiles.

Those involved in the center-based program with prepackaged meals showed the greatest average weight loss (7.9%), as compared with controls (2.1%). Both intervention groups showed statistically significant improvement in weight-loss, quality of life, leptin, carotenoid and C reactive protein levels as compared to controls. No significant interventional effects were seen in cardiopulmonary function or cholesterol profiles.

Conclusion: This study found that a weight-loss program with prepackaged foods can result in greater initial and sustained weight loss than traditional weight-loss counseling.

Rock, C., et al. Effect of a Free Prepared Meal and Incentivized Weight-Loss Program on Weight Loss and Weight Loss Maintenance in Obese and Overweight Women. **JAMA**. 2010, October 27; 304(16): 1803-1811.

PHYSICAL ACTIVITY AND GRAY MATTER IN OLDER ADULTS

Cross-sectional neuroimaging research has demonstrated that older adults who are more fit have greater volumes of gray matter than do their less fit peers. Other studies have demonstrated an increased cortical volume in response to a moderate intensity exercise regimen. This study tested whether physical activity reduces the risk of cognitive impairment.

Participants were part of the Pittsburgh component of the Cardiovascular Health Study Cognition Study (CHS-CS), a population-based, longitudinal study of coronary heart disease and stroke in persons 65 years of age or older. In this 13 year study, MRI results, physical activity and cognitive impairment were examined at study onset. Physical activity was measured as the number of blocks walked in one week. Nine years later, brain scans were obtained after the physical activity assessment for cognitively normal adults.

Two hundred ninety-nine cognitively normal subjects were identified at nine-year follow-up. Of these, 183 remained cognitively normal at the final, 13-year follow-up. The MRIs of subjects with higher physical activity demonstrated greater volumes in the frontal, occipital, and hippocampal regions. After dividing activity into quartiles, the gray matter volume in the highest quartile was greater than that of the other three quartiles (all $p < 0.05$).

Physical activity was marginally related to a reduced risk of cognitive impairment 13 years later ($p < 0.07$). Measures of gray matter volume were not predictive of cognitive impairment. However, greater volumes in the inferior frontal gyrus, hippocampal formation and supplementary motor area were associated with a reduced risk of developing cognitive impairment ($p < 0.01$, $p < 0.0009$, and $p < 0.01$, respectively).

Conclusion: This study found that greater amounts of walking are associated with greater volumes of gray matter, further associated with a reduced risk of cognitive impairment.

Erickson, K., et al. Physical Activity Predicts Gray Matter Volume in Late Adulthood: The Cardiovascular Health Study. **Neuro**. 2010, October 19; 75(16): 1415-1422.

FACTOR XA INHIBITOR FOR THE TREATMENT OF SUPERFICIAL VEIN THROMBOSIS IN THE LEG

Superficial vein thrombosis (SVT) of the legs is a common condition. Patients with isolated SVT are at risk for subsequent symptomatic venous thromboembolic events. None of the published studies has shown a clinically relevant benefit of any treatment when compared with placebo. This study was designed to assess the efficacy and safety of a factor Xa inhibitor (fondaparinux) in reducing symptomatic complications of superficial vein thrombosis.

This study included 3,002 patients diagnosed with symptomatic or limb superficial vein thrombosis at least 5 cm in length. The patients were randomly assigned in a one-to-one ratio to fondaparinux at a dose of 2.5 mg or to a matching placebo, each given once daily for 45 days. The primary outcome measure was the composite of death from any cause, symptomatic pulmonary embolism,

symptomatic deep vein thrombosis, or symptomatic extension of the thrombosis. The main safety outcome was major bleeding.

The primary efficacy outcome occurred in 13 of the 1,502 patients in the fondaparinux group, and in 88 of the 1,600 patients in the placebo group ($p < 0.001$). The treatment effect was consistent across all subtypes examined. By day 47, major bleeding had occurred in one patient in each group

Conclusion: This study of patients with superficial vein thrombosis of the leg found that a factor Xa inhibitor, fondaparinux, can significantly reduce the risk of death, clot extension, pulmonary embolism and deep vein thrombosis.

Herve, D., et al. Fondaparinux for the Treatment of Superficial Vein Thrombosis in the Legs. **N Eng J Med**. 2010, Sept 23; 363: 1222-1232.

CHANGE IN DISABILITY AFTER HOSPITALIZATION IN OLDER PERSONS

Among older persons, disability in essential activities of daily living is commonly associated with increased mortality and institutionalization as well as a greater use of home services. Disability is thought to arise when a vulnerable host is exposed to a new or worsening insult or intervening event. This study evaluated the association between intervening events and transitions among various states of disability and death.

Participants were members of the Precipitating Events Project, an ongoing longitudinal study of 754 community living persons age 70 years or older. All were initially nondisabled. Comprehensive, home based assessments were completed at baseline and at 18-month intervals for 108 months. Telephone interviews were completed monthly to assess disability and to identify exposure to intervening events. These events included illnesses and injuries leading to either hospitalization or restrictions in activity. During the telephone interviews, participants were assessed for disability using standard questions regarding essential activities of daily living.

Of the 754 participants, 15.5% made no transitions. Among the 637 participants who made at least one

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functional transition, 578 (90.7%) had at least one hospital admission, and 601 (94.3%) had at least one month of restricted activity during a median follow-up period of 102 months. Hospitalization was strongly associated with eight of the nine possible transitions. Restricted activity was also found to increase the likelihood of transitioning from no disability to both mild and severe disability, and from mild disability to severe disability. Among the possible reasons for hospitalization, fall related injury resulted in the highest likelihood of developing new or worsened disability.

Conclusion: This study found that, among older persons, injuries and illnesses significantly increase the likelihood of developing new or worsening functional disability.

Gill, T., et al. Changing Disability after Hospitalization or Restricted Activity in Older Persons. **JAMA.** 2010, November 3; 304(17): 17 1919-1928.

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